

## REMARKS

Claims 1-95 were filed in the original application. Claims 1-17, 24, 34-48, 50-56, 59-63, 65-68, 70-73, and 75-96 were cancelled in the Amendment and Response to Office Action mailed February 15, 2005, while reserving the right to prosecute these or similar claims in the future.

Thus, Claims 18-23, 25-33, 49, 57-58, 64, 69 and 74 are pending in the present application.

### **I. The Claims are Not Obvious**

The Examiner rejected claims 18-23, 25-33, 49, 57-58, 64, 69 and 74 under 35 U.S.C. § 103 (a), as being unpatentable over Zelinka (U.S. Patent No. 4,598,049). Specifically, the Examiner alleges that "it would have been obvious to one of the ordinary skill in this art at the time of the invention by applicant to modify the system of Zelinka such that there are three or more reaction chambers in order to optimize the throughput of the apparatus."<sup>1</sup> Applicants respectfully disagree.

A *prima facie* case of obviousness requires the Examiner to provide a reference which (a) discloses all of the elements of the claimed invention, (b) suggests or motivates one skilled in the art to combine the claimed elements to produce the claimed combination, and (c) provides a reasonable expectation of success should the claimed combination be carried out. Failure to establish any one of these three requirements precludes a finding of a *prima facie* case of obviousness and without more entitles the Applicant to allowance of the claims in issue.<sup>2</sup> Applicants respectfully submit that the reference cited by the Examiner does not disclose each element of the present invention, lacks reference to and discussion of a motivation to modify the cited art to produce the claimed invention of the pending application, and, therefore, does not provide a reasonable expectation that the claimed invention of the pending application would be successful.

#### **A) Zelinka (U.S. Patent No. 4,598,049) does not disclose each element of the present invention**

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<sup>1</sup> Office Action mailed November 4, 2005, page 5, lines 9-11.

<sup>2</sup> See, e.g., *Northern Telecom Inc. v. Datapoint Corp.*, 15 USPQ2d 1321, 1323 (Fed. Cir. 1990).

Zelinka does not teach or disclose all elements of the present invention. Specifically, Zelinka does not teach or disclose a plurality of reagent dispensers configured to simultaneously form closed fluidic connections with each reaction chamber. Furthermore, Zelinka does not teach or disclose reagent dispensers comprising connections to a plurality of reagent delivery lines, let alone where each reagent dispenser is connected to the reagent delivery lines.

**B) Zelinka (U.S. Patent No. 4,598,049) provides no motivation to modify a synthesizer described therein to produce a synthesizer claimed in the pending application**

Zelinka provides no suggestion or motivation to modify a synthesizer described therein (e.g., comprising a single reaction chamber) in order to produce a synthesizer claimed in the pending application. Specifically, Zelinka does not suggest or disclose any reason one would be motivated to generate a synthesizer comprising a plurality of reagent dispensers: 1) configured to simultaneously form closed fluidic connections with each reaction chamber; and 2) comprising connections to a plurality of reagent delivery lines. Thus, absent from Zelinka is a discussion or reference to how one would modify an apparatus of Zelinka (e.g., comprising a single reaction chamber) for the controlled delivery of reagents to more than one reaction cell.

If one were to take a synthesizer described in Zelinka and attempt to modify it in order to create a synthesizer comprising a plurality of reaction chambers, one would use the teachings of Zelinka to do so. Thus, using the teachings of Zelinka<sup>3</sup>, one would attempt to generate a synthesizer with a plurality of reaction chambers that comprised a plurality of syringes and valves for controlled delivery of reagents to each reaction chamber. One would not, using the teachings of Zelinka, generate a synthesizer described and claimed in the pending application (e.g., comprising a plurality of reagent dispensers: 1) configured to simultaneously form closed fluidic connections with each reaction chamber; and 2) comprising connections to a plurality of reagent delivery lines).

Thus, Zelinka does not provide a suggestion or motivation to alter a synthesizer described therein (e.g., comprising a single reaction chamber) in order to produce a synthesizer claimed in the pending application.

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<sup>3</sup> In reality, Zelinka provides no description of how one would modify a device of Zelinka for the controlled delivery of reagents to more than one reaction chamber.

**C) The Reference Does Not Provide a Reasonable Expectation of Success**

Failure of Zelinka to provide a suggestion or motivation to modify an apparatus described therein (e.g., to incorporate elements of the present invention) can be attributable to Zelinka's lack of foresight regarding, and description of, technical difficulties encountered with a plurality of reaction chambers, reagent dispensers and reagent delivery lines. Specifically, Zelinka fails to provide any insight or solution regarding: 1) the challenge of delivering reagents to a plurality of reaction chambers (e.g., in order to simultaneously generate a plurality of different oligonucleotides); 2) synthesis performance failure (e.g., caused by changes in pressure within the synthesizer of Zelinka); as well as 3) the accumulation of hazardous waste, biohazard and environmental contamination issues resulting from use of a synthesizer comprising a plurality of reaction chambers.

The Federal Circuit has made it very clear that one must determine whether "the prior art would have suggested to one of ordinary skill in the art that [a] process **should** be carried out and **would** have a reasonable likelihood of success, viewed in light of the prior art."<sup>4</sup> There is no reasonable expectation of success because there was no way to predict what configuration, if any, using a synthesizer of Zelinka would have worked (e.g., would have overcome the technical hurdles mentioned above) for parallel synthesis with three or more reaction chambers.

Although the examiner echoes the allegation made within Zelinka that conceivably a number of reaction cells could be coupled to the apparatus so as to optimize the through-put of the apparatus, Zelinka (and the Examiner) neglects to acknowledge (e.g., to discuss or reference) complexities and technical challenges involved with the controlled delivery of reagents to a plurality of reaction chambers. Specifically, Zelinka does not describe, or reference, how one would adapt a synthesizer described in Zelinka for the controlled delivery of reagents to more than one reaction chamber using a system of syringes and valves disclosed in Zelinka. Thus, one could not reasonably expect that a plurality of different oligonucleotides could be generated simultaneously using the system of Zelinka (e.g., using a plurality of reagent dispensers).<sup>5</sup>

Zelinka also fails to address how a synthesizer comprising a plurality of reaction chambers could be configured so as to overcome performance failures arising within a

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<sup>4</sup> *In re Dow Chemical*, 5 USPQ2d 1529, at 1532 (Fed. Cir. 1988) (Emphasis added).

<sup>5</sup> In contrast, the presently claimed invention does in fact overcome this hurdle by providing a synthesizer configured to simultaneously form closed fluidic connections with each of a plurality of reaction chambers thereby permitting parallel synthesis of distinct polymers.

synthesizer comprising more than one reaction chamber (e.g., pressure changes affecting delivery of reagents to each reaction chamber), and fails to address environmental contamination issues. Specifically, Zelinka fails to provide guidance as to how changes in pressure within a synthesizer (e.g., after controlled delivery of heat to the system) could be stabilized (e.g., permitting accurate and desired delivery of reagents to a reaction chamber). Furthermore, Zelinka fails to address how hazardous waste is to be safely removed from a plurality of reaction chambers.<sup>6</sup>

Thus, not only does Zelinka lack any discussion or reference as to how a synthesizer therein (e.g., comprising a single reaction chamber) could be altered to generate a synthesizer comprising a plurality of reaction chambers, Zelinka also fails to provide a reasonable expectation that a synthesizer of the present invention (e.g., comprising a plurality of reagent dispensers: 1) configured to simultaneously form closed fluidic connections with each reaction chamber; and 2) comprising connections to a plurality of reagent delivery lines) could be manufactured and utilized for the parallel synthesis of distinct polymers.

Accordingly, it is respectfully submitted that the examiner has not met the requirements of establishing a prima facie case of obviousness. Applicants respectfully request that this ground of rejection be removed and the pending claims be passed to allowance.


## CONCLUSION

For the reasons set forth above, it is respectfully submitted that Applicants have addressed all grounds for rejection and Applicants' claims should be passed to allowance. Reconsideration of the application is respectfully requested. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourages the Examiner to call the undersigned collect at (608) 218-6900.

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<sup>6</sup> In contrast, both of these technical hurdles are overcome in the pending application. For example, the present invention comprises a closed fluidic system that enables a central reagent supply to deliver reagents at a constant and controlled pressure to each of a plurality of reagent delivery lines (e.g., each delivery line can be individually pressurized) (See, e.g., Specification, pages 16-17, lines 20-31 and lines 1-5, respectively, and page 26, lines 9-11). In addition, the closed system of the present invention was developed and configured to overcome hazardous waste and environmental issues in that the synthesizer permits waste removal from the reaction chambers without exposure to the ambient environment (See, e.g., Specification at pages 16-17, lines 20-31 and 1-5, respectively).

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